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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WORTMAN, DONNA C	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/029,840	MENG ET AL.	
	Examiner	Art Unit	
	Donna C. Wortman, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *4,5,7 and 14-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6 and 8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on _____ is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,8,15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's election with traverse of Group I, claims 1, 2, 6 and 8-13 in Paper No. 16 is acknowledged. The traversal is on the ground(s) that searching for the nucleotide sequences of Groups II-VI will require the same search as the search for Group I and that the sequences of Groups II-VI are fragments of the SEQ ID NO:1, which is claimed in Group I; that Groups VII-X and XII comprise protein species that are encoded by the nucleotide sequences of Groups I-VI and can reasonably be examined together; and that the remaining groups are related and/or that some of the searches are likely to overlap. This is not found persuasive because subsequences of nucleotide sequences or of protein sequences require separate searches; because a search for viral proteins does not require use of or search for nucleotide sequences; and because overlapping or related searches need not be coextensive.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's attention is hereby directed to the following citation of M.P.E.P. §821.04 regarding the restriction of claims to a product and processes of using the product and rejoinder:

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02(c) and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.
>
> In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104 - 1.106. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. If the application containing

> the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a citation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. §103(b)" (1184 TMOG 86(March 26, 1996)):

> "However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all the limitations of** an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

In accordance with M.P.E.P. §821.04 and In re Ochiai, 71 F.3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product claims will occur following a finding that the product claims are allowable. Until such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

The possibility of rejoinder appears to exist with respect to the claims of Group XIII and XIV if they are amended to maintain either dependency on the product claims or to otherwise include the limitations of the product claims of Group I, which now includes original Group II.

On further consideration, Group II, claim 3 in part (part a and b, SEQ ID NO:1), is rejoined to Group I and will be examined. Claims 1, 2, 3 (in part), 6 (in part), and 8-13 are under examination as drawn to the elected invention.

Claims 2, 3 in part, 4, 5, 7, and 14-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 16.

Claims 3 and 6 are objected to because of the following informalities: Claims 3 and 6 are objected to as reciting non-elected inventions: Claim 3, part (c) recites immunogenic fragments, and claim 6 recites "an antigenic protein." Appropriate correction is required.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6 and 8-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in reciting "An isolated avian hepatitis E virus having no more than about 80% nucleotide sequence identity to an Australian big liver and spleen disease virus." Since no particular Australian big liver and spleen disease virus isolate or nucleotide sequence is specified, one would not know how to define "no more than about 80% nucleotide sequence identity" to an unspecified virus or nucleotide sequence.

Claim 2 is indefinite in reciting "has a nucleotide sequence set forth in SEQ ID NO:1." It is not clear what or what size sequence is encompassed, since "a" sequence set forth in SEQ ID NO:1 could mean as little as two or three nucleotides of SEQ ID NO:1.

Claim 3 is similarly indefinite in reciting, in part (a), "a nucleotide sequence set forth in SEQ ID NO:1" and, in part (b), "a nucleotide sequence that hybridizes to and which is at least 90% complementary to the nucleotide sequence set forth in SEQ ID NO:1" since it is not clear what size sequence is encompassed by "a" nucleotide sequence.

Claims 6 and 8 are also indefinite in reciting "a" nucleotide sequence.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claim 1 encompasses a genus of avian hepatitis E viruses that have no more than about 80% polynucleotide sequence identity to an unspecified Australian big liver and spleen disease virus. The specification describes a single species, an avian hepatitis E viral isolate whose genomic polynucleotide sequence is represented by SEQ ID NO:1. The written description requirement for a claimed genus

may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 19 F.3d at 1568, 43 USPQ2d at 1406. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See, e.g., Eli Lilly. Since the actual range of variability in the genus encompassed by claim 1 is extensive, and since necessary common attributes or features of the elements possessed by the members of the genus in view of the single species disclosed are not described, claim 1 contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Please see MPEP 2163.

Claims 8-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising an isolated avian hepatitis E virus having the nucleotide sequence set forth in SEQ ID NO:1, does not reasonably provide enablement for a vaccine comprising isolated avian hepatitis E virus that confers protection against a viral infection or disease, or for a method of vaccination using such a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Claims 8-13 encompass vaccines and methods that protect avian or mammalian species, including humans, against an avian or mammalian hepatitis E infection, and that encompass making and using a modified live avian hepatitis E virus, an inactivated avian hepatitis E virus, or an attenuated avian hepatitis E virus that have a nucleotide sequence set forth in SEQ ID NO:1. The specification does not enable a person skilled in the art to practice the invention throughout its scope without undue experimentation in several aspects. First, the specification does not teach that any avian hepatitis E viral vaccine, modified live, inactivated, or attenuated, is actually protective against an avian or mammalian hepatitis E infection in any species. It has not even been demonstrated that chickens that have been once infected with the virus are protected against a second infection with the same or similar virus. Second, even if it were to be established that an avian hepatitis E virus confers protection against infection, the specification does not teach how to modify, inactivate, or attenuate an avian hepatitis E virus to produce an effective vaccine for chickens. Third, the specification does not teach that any avian

hepatitis E virus--modified live, inactivated, or attenuated--would have the immunogenic properties required to produce protective immunity against a hepatitis E infection in any mammalian species. In assessing enablement, it is appropriate to take into account

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims and the nature of the invention is discussed above. With respect to the state of the prior art, the avian hepatitis E virus disclosed and claimed by Applicant is a newly characterized virus. There is no known vaccine against avian hepatitis E virus, the related Australian big liver and spleen disease virus, or swine hepatitis E virus. A recombinant subunit vaccine for human hepatitis E virus is being developed, but there is apparently no live, inactivated, or attenuated human hepatitis E virus vaccine. The direction provided in the instant specification for making and using vaccines is of a general or a prophetic type, including suggesting that attenuation can be achieved by repeated passaging through eggs, and does not involve any actual working examples. Making and using viral vaccines is generally

unpredictable, as evidenced by Fields et al., Eds., FIELDS VIROLOGY,Third Edition, Lippincott Williams & Wilkins, 1996. See, for example, pages 480-482, "Disadvantages of Nonliving-Virus Vaccines" which discloses *inter alia* that some non-living virus vaccines potentiated rather than prevented disease, possibly as a result of the inactivation treatment. Also see page 483, second paragraph, indicating that experimental systems for evaluating attenuations do not exist for every type of virus, and "Basis for Attenuation" which indicates that "satisfactorily attenuated mutants are the product of a process of genetic roulette followed by selection of mutants with the desired properties of attenuation and immunogenicity. The unpredictability of this process is illustrated by the failure of Theiler ... to produce additional attenuated mutants of yellow fever using the protocol that yielded the satisfactorily attenuated 17D strain of virus. The genetic basis for attenuation of measles, mumps, rubella, yellow fever, and vaccinia viruses is unknown, whereas the genetic determinants of attenuation of the three live-poliovirus vaccine strains have been characterized extensively." Taking into account all of the factors listed above, the specification cannot be said to enable one of skill in the art to practice the subject matter of claims 8-13 without undue experimentation.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

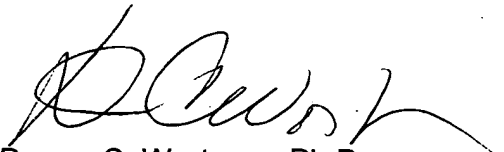
Claim 1 is rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Shivaprasad et al. (Proc. Western Poult. Dis. Conf. p. 6, Sacramento CA, 1995), cited by Applicant on PTO 1449. Shivaprasad et al. disclose the presence of viral particles in samples collected from chickens with necrohemorrhagic hepatitis and subjected to electron microscopy. Giving the language of claim 1 its broadest reasonable interpretation, "isolated" has been interpreted as encompassing virus present in samples that have been prepared for electron microscopy. Although Shivaprasad et al. did not compare any nucleotide sequences, since Shivaprasad et al. apparently collected the viral samples from chickens in the U.S., and since the viral particles were found in bile and were 30-40 nanometers in size,

just as disclosed for Applicant's virus (specification, Example 1), it reasonably appears that the virus disclosed by Shivaprasad et al. is the same as, or only slightly different from, the virus recited in claim 1.

SEQ ID NO:1 is free of the prior art. Product claims limited to a polynucleotide comprising SEQ ID NO:1 and an isolated virus comprising a polynucleotide comprising SEQ ID NO:1 would be allowable. Applicant is reminded that any rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112.Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is 703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw